

## REMARKS

Upon entry of the present amendment, claims 1 – 4, 6, 7, 11, 14 – 19, 21 – 26, and 29 – 31 are pending. Claims 5, 8 - 10, 12, 13, 20, 27, 28 and 32 – 37 have been cancelled. The present amendment adds no new matter.

### **THE NON-STATUTORY DOUBLE PATENTING REJECTION**

The Examiner has provisionally rejected claims 1, 7, 8, 10-12, 14-15, 17-19 and 24 on the grounds of non-statutory obviousness-type double patenting as being unpatentable over claims 1-7, 11, 12, and 16-19 of copending U.S. Patent Application No. 10/602340.

Upon notification of allowable subject matter, Applicants will review the need for a terminal disclaimer.

### **OBJECTION OF CLAIMS 10, 12 AND 13**

The Examiner has objected to claims 10 and 12-13 under 37 CFR 1.75(C), as being of improper dependent form for failing to further limit the subject matter of a previous claim.

Applicants have cancelled claims 10, 12 and 13. Accordingly, Applicants believe that the present rejection is now moot.

### **THE 35 U.S.C. §112, SECOND PARAGRAPH REJECTION**

The Examiner has rejected claims 10, 12 and 13 under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicants have cancelled claims 10, 12 and 13. Accordingly, Applicants believe that the present rejection is now moot.

### **THE 35 U.S.C. §103(A) REJECTION**

The Examiner has rejected claims 1-4, 6-7, 10-19, 21-26 and 29-31 under 35 U.S.C. 103(a) as being unpatentable over The Medicine Catalogue (“**The Medicine Catalogue**”) in view of Pingel *et al.* (US Patent No. 6,903,069; “**Pingel**”) and Johannessen *et al.* (WO 01/82943; “**Johannessen**”) and Perez Garcia (US Patent No. 2,145,869; “**Perez Garcia**”). Specifically, the Examiner has stated that although the difference between the present invention and **The Medicine Catalogue** is that **The**

**Medicine Catalogue** does not teach calcium salt in the concentration specified, one skilled in the art “would have been motivated to optimize the CaCl<sub>2</sub> concentration, since **Johannessen** indicates that CaCl<sub>2</sub> maintains the FVIIa activity, and is required in an amount more than 0.15mg/ml.

Applicants disagree. The present invention is directed to “a composition that comprises a calcium salt in a concentration of at least 200 mM, such that the composition is hypertonic”. Thus, the compositions of the present invention have at least 29.4 mg/ml of CaCl<sub>2</sub>. In contrast, neither **The Medicine Catalogue** nor **Johannessen** teach or suggest a composition comprising anywhere near the amount of 29.4 mg/ml of CaCl<sub>2</sub>. In fact, the prior art teaches that levels as low as 1.0 mg/ml (**Johannessen**) or 1.5 mg/ml (**The Medicine Catalogue**) were sufficient to maintain FVIIa activity. Applicants assert that a skilled artisan would not be motivated to maximize the amount of CaCl<sub>2</sub> to the level taught by the present invention, as satisfactory results would be obtained at the lower levels. However, the present invention is based on the discovery that such “hypertonic” compositions dramatically result in a decreased formation of heavy chain fragments during storage for as long as six months. *See e.g.* Examples 7 and 9. For instance, such “hypertonic” compositions have over 50% less heavy chain fragments than compositions as such those taught in the art (*i.e.* those having approximately 1.5 mg/ml of CaCl<sub>2</sub>; composition 1 of Example 7 and formulation A of Example 9). Thus, Applicants assert that the present invention is not based upon the optimization of known ranges within the art by routine experimentation, but instead the discovery of a critical aspect of maintaining the stability of such Factor VII formulations. Moreover, Applicants assert that the prolonged stability of such Factor VII compositions is critical to the functionality of such a therapeutic. Accordingly, in light of the arguments above, Applicants request reconsideration and withdrawal of the present invention.

### Conclusion

In view of the above, Applicant(s) submit(s) that the application is now in condition for allowance and issue and respectfully request(s) early action to that end. Applicant(s) believe(s) that no additional fees are due. However, should any fees be due, the Commissioner is hereby authorized to charge any fees in connection with this application and to credit any overpayments to Deposit Account No. 14-1447. The undersigned invites the Examiner to contact her by telephone if there are any questions concerning this amendment or application.

Respectfully submitted,

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**/Shelby J. Walker, Reg. No. 45,192/**

Shelby J. Walker, Reg. No. 45,192

Novo Nordisk Inc.

Customer Number 23650

(609) 987-4883